REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. Claim Status and Amendments

Claims 16-30 were pending in this application when last examined and stand rejected.

Claim 16 is amended to include positive method by incorporating the subject matter of claims 21 and 28, which are now cancelled without prejudice or disclaimer thereto.

To better conform to US practice, claim 16 is amended to remove the method of treatment aspect of the claim, which has added back in new independent claim 31. Accordingly, amended claim 16 is now directed to a method of *in vitro* diagnosis of pathologies linked to over-expression of GLUT1 on cell surfaces, whereas new claim 31 is directed to the method for prevention or treatment of pathologies linked to over-expression of GLUT1 on cell surfaces.

Claims 16-19, 24, and 29-32 are amended in a non-narrowing manner to make minor editorial revisions to better conform to U.S. claim form and practice. Such revisions are non-substantive and not intended to narrow the scope of protection. The revisions include: replacing the "characterized by" language with "wherein"; revising the beginning of the claims to recite "A" or "The"; revising the

claim language to provide proper antecedent basis throughout the claims; and revising the claims to use proper alternative language.

Claim 29 is amended to change its dependency to claim 31. Claim 30 is amended to a proper independent claim.

No new matter has been added by the above claim amendments.

Claims 21-24 and 28 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claims 16-20, 25-27, and 29-31 are pending upon entry of this amendment.

II. Indefiniteness Rejection and Rejection under 35 USC 101

Claims 16-20 and 22-24 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to recite positive method steps for the reasons on page 2 of the Office Action. For the same reasons, claims 16-20 and 22-24 were rejected under 35 U.S.C. § 101, as being improper definition of a process on page 2 of the Office Action.

The present amendment overcomes these rejections by amending the claims to set forth the proper method steps. Thus, the amended claims are believed to be clear, definite,

and proper process claims. Withdrawal of the rejections is requested.

III. Enablement Rejection

Claims 16-29 were rejected under 35 U.S.C. § 112 on the basis the specification that the specification is enabling for a method of in vitro diagnosis of cells over-expressing GLUT1 peptide on cell surfaces and diagnosing tumors, but not for preventing or treating pathologies, targeting drugs, or diagnosing the other recited conditions. See pages 2-4 of the Office Action. This rejection is traversed as applied to the amended claims.

It seems the Office is concerned with how to diagnose a GLUT1 deficiency syndrome by detecting an overexpression of GLUT1 and how to prevent or treat pathologies.

The test of enablement is whether one reasonably skilled in the art could make or use the invention based on the disclosure in the specification coupled with the knowledge in the art without undue experimentation. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2164.01 and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the instant case, it is respectfully submitted that the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, could diagnose a GLUT1 deficiency syndrome by detecting an overexpression of GLUT1 the skilled artisan could prevent or treat said pathologies by using the routine techniques and procedures without undue experimentation.

Applicants will start by discussing the method for the *in vitro* diagnosis of the pathologies recited in the claims.

Different cancers

As to different cancers, the over-expression of GLUT1 is already used in oncologic diagnostics, for example, by measuring the consumption of a fluoro derivate of glucose. In fact, as recognized by the Examiner, the state of the art contains considerable knowledge about the relationship between elevated glucose consumption and presence of tumor tissue in biopsies as indicated on page 3, lines 10-12 of the Office Action. In the state of the art, the aberrant glucose consumption is monitored by the synthetic component FDG (fluorodeoxyglucose). In connection with imaging technique, this component enables one skilled in the art to diagnose the tumor tissue and to establish a detection threshold by studying the relationship of signals in a positive or negative

zone of a tissue section and by comparing the signals between different sections.

In view of the forgoing and based on the guidance in the disclosure, it is believed that the GLUT1 binding polypeptides described in the present application could indeed be used to diagnose tumor tissue existence according to the same principle in connection with imaging technique as what is already established in the field. See the attached picture of annex 1, which represents a cerebral tumor section marked by the GLUT1 binding polypeptides of the present application. This picture clearly displays positive zones in green which correspond to tumor tissues and a negative background that corresponds to normal tissue.

Inflammatory conditions

The prior study of Applicants has shown that GLUT1 expression is induced by T cell activation (Reference 1: Manel et al., Blood, Vol. 101., No. 5, 1913-1918, 2003, attached herewith). So, GLUT1 expression has been linked to inflammatory conditions. Different inflammatory cells, such as lymphocytes, macrophages or microglias in a biopsy can be distinguished by an aberrantly high GLUT1 expression.

GLUT1 expression *in vivo* can be directly detected by a blood sample analysis, wherein the mononuclear cells contained in a buffy coat are marked by the GLUT1 binding polypeptides described in the present application and analyzed

by FACS (Fluorescence Activated Cell Sorting). Accordingly, the presence of highly marked cells would indicate inflammatory conditions.

GLUT1 expression can also be monitored in connection with imaging technique. As shown in the attached picture of Annex 2, the GLUT1 positive inflammatory cells are well distinguished from GLUT1 negative proliferative basal cells in the situation of malignancy.

In view of the forgoing and based on the guidance in the disclosure, it is believed that the GLUT1 binding polypeptides described in the present application could indeed be used to diagnose inflammatory conditions according to the above-noted principles using routine imaging techniques and procedures without undue experimentation.

Prevention or Treatment

As to the method for the prevention or the treatment of the pathologies recited in the claims, the specification discloses that glucose transportation through GLUT1 can be inhibited by the binding of certain polypeptides to a receptor, especially the polypeptides coming from the HTLV receptor binding domain (RBD) as reported in Applicants' prior publication (Reference 2: Manel et al., Cell, vol. 115, 449-459, 2003 fig.1(E), attached herewith).

Since the accessibility of an infecting retrovirus to a retroviral receptor could be blocked by a competing

ligand, this kind of ligand, such as the GLUT1 polypeptides of the claims for the present application could similarly be used as a conceivable antiviral agent.

With regard to side effects from systemic inhibition, one skilled in the art would easily predict what the side effects might be based on his general medical knowledge.

In view of the forgoing and based on the guidance in the disclosure, it is believed that the GLUT1 binding polypeptides described in the present application could indeed be used to treat the pathologies recited in the claims following routine procedures without undue experimentation.

For the above-reasons, it is respectfully submitted that the specification enables the full scope of the claims. Therefore, withdrawal of the enablement rejection is requested.

IV. Prior Art Rejection

Claim 30 was rejected under 35 U.S.C. § 102(b) as being anticipated by Palker et al. (Journal of Virological Methods, 18:243-255, 1987) for the reasons on pages 4-5 of the Office Action. This rejection is respectfully traversed.

Palker et al. discloses the entire extracellular surface component of HTLV and detection of anti-HTLV antibodies. However, Palker et al. never mentions any special peptide sequences having the claimed activity, for example to specifically recognize GLUT1.

Further, the skilled artisan knows that the entire extracellular surface component of HTLV can fix to other factors, such as, heparin sulphate, neurophlin 1 or Hsc70, other than GLUT1. A polypeptide specially binding to a specific protein is completely different from an entire protein complex upon which can fix several kinds of biological molecules.

It is clear that a single component, such as the GLUT1 binding polypeptide in claim 30 is different from the gp46 of HTLV-1 in Palker et al. For this reason, the rejection should fall, because Palker et al. fails to disclose the GLUT1 binding polypeptide of the claims.

Withdrawal of the rejection is requested.

V. Information Disclosure Statement

On page 5 of the Office Action, it was indicated that the Information Disclosure Statement (IDS) filed November 2, 2005 was not considered on the basis that Applicants did not provide legible copies of each cited foreign patent document and each non-patent literature publication to the Office.

Applicants respectfully disagree and submit that the references should have been officially considered by the Office, because copies of the references should have been forwarded to the USPTO by the International Search Authority

pursuant to the trilateral agreement between the USPTO, EPO and JPO. Thus, the references should have been considered as they should be of record at the USPTO.

Nonetheless, for the convenience of the Office, Applicants have attached copies of the non-patent literature references herewith. Kindly consider the references listed on the IDS of November 2, 2005 and return an Examiner-initialed copy of PTO-1449 form indicating such.

VI. Conclusion

Having addressed all the outstanding issues, the amendment is believed to be fully responsive. The application is believed to be in condition for allowance and notice to that effect is requested. If the Examiner has any proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Charge the fee of $220 for the one independent claim added herewith to our credit card.

The Commissioner is hereby authorized to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item(s):

☒ - Annex 1

☒ - Annex 2

☒ - Reference 1: Manel et al. Blood 2003, Vol. 101., N° 5, 1913-1918

☒ - Reference 2: Manel et al. Cell, vol. 115, 449-459, fig1E

☒ - copies of non-patent literature references submitted in the IDS of November 2, 2005.